UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,550	06/18/2001	William E. Marshall	P01936US5	1897

22885 7590 05/09/2006

MCKEE, VOORHEES & SEASE, P.L.C.
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/883,550	**Applicant(s)** MARSHALL, WILLIAM E.	
	Examiner Robert A. Zeman	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 April 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): see attached.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,4-8,10-12 and 14-19*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

ADVISORY ACTION

The amendment and response filed on 4-24-2006 are acknowledged. Claim 1 has been amended. Claim 13 has been canceled. Claims 1, 4-8, 10-12 and 14-19 are pending and currently under examination.

Claim Rejections Withdrawn

The new matter rejection of claims 1, 4-8 and 10-19 under 35 U.S.C. 112, first paragraph, based on claim 1 reciting the limitation "quantifying an amount of SRFs present in said filtrate by determining an absorbance at a wavelength of 254 nanometers (nm)" is withdrawn in light of the amendment to claim 1.

The new matter rejection of claim 13 under 35 U.S.C. 112, first paragraph, based on claim 13 reciting the limitation "administering the amount of SRFs from about 1000 to 24000 AU of said SRFs/mL as determined at wavelength of 254 nanometers" is withdrawn. Cancellation of said claim has rendered the rejection moot.

The rejection of claim 13 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "as determined at wavelength of 254 nanometers" is withdrawn. Cancellation of said claim has rendered the rejection moot.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1, 4-8, 10-11, 14-15 and 17-19 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al. (Microbiology, Vol. 142, 1996, pages 817-827) is maintained for reasons of record. The cancellation of claim 13 has rendered the rejection of that claim moot. Moreover, claims 12 and 16 were inadvertently included in this rejection and have been removed.

Applicant argues:

1. De Vuyst et al. does not teach bacteriocins are released from bacteria as 6 kDa proteins.

2. De Vuyst et al. disclose that the molecular weight of bacteriocins under native conditions exceeds 30kDa.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion, the bacteriocins disclosed by De Vuyst et al. are not limited to the aggregate form. In fact, De Vuyst et al. disclose that to harvest maximum bacteriocin levels it is advisable to use conditions that prevent aggregation (see page 824, right hand column). Consequently, De Vuyst et al. disclose bacteriocins comprising the 6 kDa monomers that meet the limitations of the instant claims.

As outlined previously, De Vuyst et al. disclose methods of producing low molecular weight proteins from bacteria by subjecting them to a number of stresses. By definition, these proteins are stress response factors. These stresses include: a change in temperature, a change in pH, a change in biomass (crowding or decreasing the amount of media), and adding toxins such as ethanol (see abstract). Subjecting the lactic acid bacteria to any of these stressors results in the

release of low molecular weight monomers of bacteriocin (approx 6 kDa or less) that oligomerize to be about 30 kDa. De Vuyst et al. remove components larger than the bacteriocin monomer (see page 818, column 1). De Vuyst et al. further disclose that these bacteriocins are able to kill or harm other bacterial species and suggest the use of said bacteriocins as food additives (see page 818, column 1). Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have followed the suggestion of De Vuyst et al. and administer the low molecular weight proteins produced by stressed bacteria to animals since said proteins (bacteriocins) can act to kill or render harmless other strains of bacteria and thereby enhancing the ability of an animal's immune system to deal with bacterial infections minimizing the complications associated with introducing a bacterial strain into the normal flora of an animal. Moreover, the internalization of said proteins by an animal would stimulate its the immune system.

Moreover, the instant claims are drawn to **all** factors produced with a molecular weight less than 10 kDa in response to nutrient deprivation. The amendment to claim 1 provides no correlation between the measured absorbance and the amount of SRFs present in the filtrate.

The rejection of claims 1, 4-8, 10-15 and 17-19 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Nanji (U.S. Patent 5,413,785 – IDS-2) is maintained for reasons of record.

Applicant argues:

1. De Vuyst et al. and Nanji don't teach all the elements of the claimed invention as neither teaches a stress release product with a molecular weight of less than 10 kDa.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion, the bacteriocins disclosed by De Vuyst et al. are not limited to the aggregate form. In fact, De Vuyst et al. disclose that to harvest maximum bacteriocin levels it is advisable to use conditions that prevent aggregation (see page 824, right hand column). Consequently, De Vuyst et al. disclose bacteriocins comprising the 6 kDa monomers that meet the limitations of the instant claims.

As outlined previously, De Vuyst et al. disclose methods for producing low molecular weight proteins from stressed bacteria (bacteriocins) and suggests adding said proteins to food (see above). Nanji discloses the administration of lactic acid bacteria to humans, livestock and other animals for protection against endotoxin-mediated shock. Nanji further discloses that said bacteria should be able to produce anti-microbial substances and/or produce proteinaceous antagonistic substances (bacteriocins) since said substances aid in preventing the growth of gram-positive and gram-negative bacteria in the intestine and thereby reducing endotoxin formation (see column 10, lines 40-45). Reduction of endotoxin levels, in turn, reduces the effects of said endotoxin on the immune processes of the animal. Therefore, it would have been obvious to one of ordinary skill in the art to use the bacteriocins disclosed by De Vuyst et al. in the treatment methodologies of Nanji in order to take advantage of the immune enhancing effects of the bacteriocins while minimizing the complications associated with introducing a bacterial strain into the normal flora of an animal. One would have had a high expectation of success since De Vuyst et al. disclose the use of said bacteriocins as a food additive and Nunji disclose the importance of bacteriocins in reducing endotoxin levels and thereby reducing the deleterious effects of said endotoxin on the animal's immune system.

Moreover, the instant claims are drawn to **all** factors produced with a molecular weight less than 10 kDa in response to nutrient deprivation. The amendment to claim 1 provides no correlation between the measured absorbance and the amount of SRFs present in the filtrate

The rejection of claim 16 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Perdigon et al. (Journal of Food Protection Vol. 53, No. 5, pages 404-410, 1996 – IDS-2) is maintained for reasons of record.

Applicant argues:

1. De Vuyst et al. and Nanji don't teach all the elements of the claimed invention as neither teaches a stress release product with a molecular weight of less than 10 kDa.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion, the bacteriocins disclosed by De Vuyst et al. are not limited to the aggregate form. In fact, De Vuyst et al. disclose that to harvest maximum bacteriocin levels it is advisable to use conditions that prevent aggregation (see page 824, right hand column). Consequently, De Vuyst et al. disclose bacteriocins comprising the 6 kDa monomers that meet the limitations of the instant claims.

The teachings of De Vuyst et al. are discussed above. Perdigon et al. disclose the use of lactic acid bacteria and the proteins produced therein as immunogens and adjuvants in the generation of protection from enteropathogens (see abstract, page 404, column 2 and pages 408-409). It would have been obvious to one of ordinary skill in the art at the time the invention was made to **use the low molecular weight proteins disclosed by De Vuyst et al. as adjuvants** for the induction of a immune response to another co-administered pathogen since Perdigon et al.

discusses the use of lactic acid bacteria (and the proteins produced by said bacteria) as adjuvants for enteropathogens (an increased immune response to said enteropathogens was also disclosed) and De Vuyst et al. disclose that proteins produced by lactic acid bacteria have an immunomodulatory effect. Consequently, since the lactic acid bacteria serve as the immunogen, they do not need to be separated from the milk in order to meet the limitations of the rejected claim.

Moreover, the instant claims are drawn to **all** factors produced with a molecular weight less than 10 kDa in response to nutrient deprivation. The amendment to claim 1 provides no correlation between the measured absorbance and the amount of SRFs present in the filtrate.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ROBERT ZEMAN
PATENT EXAMINER

May 3, 2006